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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/902,460 | 07/09/2001 | John C. Fiddes | 004973-078 | 7479 |
| 7590 06/02/2004 | | | | |
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| Alexandria, VA 22313-1404 | | | | |
| | | EXAMINER | | |
| | | SAUD, CHRISTINE J | | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1647 | | |

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/902,460

Applicant(s)

FIDDES ET AL.

Examiner

Christine J. Saoud

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 12-28 is/are pending in the application.
- 4a) Of the above claim(s) 12-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 100501.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of FGF variant having the substitution K128S (claims 1-7 reading on the elected invention) in Paper filed 12 September 2003 is acknowledged.

Claims 12-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 12 September 2003.

Priority

It is noted that the instant application has an extensive patent application history, with a number of continuation-in-part applications. A review of some of the patent applications in the patent family indicate that priority for the claimed subject matter (bFGF analogs which comprise substitutions in the region of amino acids 128-138) reaches at least back to U.S. Pat. Application No. 07/459,739 (02/12/90), but not back to 06/809,163 (filed 12/16/95). Art will be applied according to this date. Applicant is invited to provide evidence of an earlier filing date if necessary.

Claim Objections

Claims 1-7 are objected to because of the following informalities: they include non-elected subject matter. The claims should be limited to substitutions in the region of 128-138 of bFGF (the elected invention). Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are directed to "DNA sequence", however, this is not statutory subject matter. A "DNA sequence" is merely a representation of a nucleic acid molecule in written form, and not the actual composition of matter. Therefore, in order to overcome the rejection, it is suggested that Applicant claim a "DNA molecule" or something similar which reflects the actual invention which is to be patented.

Additionally, the claimed invention is directed to non-statutory subject matter because it encompasses a product of nature. The recitation of "recombinant" does not distinguish the claimed DNA from a DNA which would be found in nature because all DNA is "recombinant". In the absence of a recitation of "isolated" or some other recitation to indicate the "hand of man", the claimed invention is non-statutory.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because they fail to point out what is included or excluded by the claim language of "analog". This claim is an omnibus type claim. The recitation of "analog" without a recitation of function implies any DNA sequence encoding something that differs from "mammalian FGF". Because there is no indication of the starting material, any one mammalian FGF would differ from another, and thereby constitute an "analog" (such as bovine and human bFGF or aFGF and bFGF).

Additionally, any DNA which could be made with a mammalian FGF as the starting material could be considered an "analog", and therefore, since any DNA would hybridize to a particular DNA under very low stringency conditions, every DNA in existence could conceivably be encompassed by the claims. Therefore, the claims fail to point out what is included or excluded by the claim language of "analog" and the claims are deemed to be indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding human basic FGF having a reduced affinity for heparin binding wherein the protein comprises a

Art Unit: 1647

substitution of a positively charged amino acid residue within the region of amino acids 128-138 with a neutral or negatively charged amino acid, does not reasonably provide enablement for any bFGF protein analog with reduced affinity for heparin binding. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification discloses that there are particular domains found in human basic fibroblast growth factor (bFGF) which are responsible for heparin binding. The specification speculates that positively charged amino acids in these heparin binding domains are responsible for binding of the protein to heparin. The specification asserts that substitution of a positively charged amino acid in a heparin binding domain with a neutral or negatively charged amino acid will reduce the binding affinity of the bFGF protein for heparin. However, the instant claims encompass any analog with reduced affinity for heparin binding. The instant specification does not provide guidance as to which other regions of bFGF would be likely to contribute to heparin binding, and therefore, should be modified in order to obtain a protein with the claimed biological activity. Whereas one of ordinary skill in the art could envision that there would be other modifications that could be made in the bFGF molecule and result in a reduced binding affinity for heparin, where these modifications could be made and how they should be made is only a guess and a trial and error process. This is not an enabling disclosure. The specification provides preferred mutations at positions 128, 129, 134 and 138, but no other guidance is provided in the instant specification. Therefore, it would appear

Art Unit: 1647

that undue experimentation would be required to determine which other regions could and should be mutated to create a human bFGF analog with reduced binding affinity for heparin, absent evidence to the contrary.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Baird et al. (Rec. Prog. Horm. Res. 42: 143-205, 1986).

Baird et al. teach a number of analogs of bFGF, including peptides of bFGF (see Table 1 at page 158). Because some of the peptides lack the heparin binding domain of amino acids 128-138, these peptides would also possess a reduced affinity for heparin binding. Therefore, the claims are anticipated by the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

Art Unit: 1647

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**CHRISTINE J. SAUD
PRIMARY EXAMINER**

Christine J. Saud